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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/781,499 | 02/18/2004 | Michel Chateau | 34076/US | 6087 |

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| DORSEY & WHITNEY LLP | | |
| INTELLECTUAL PROPERTY DEPARTMENT | | |
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| EXAMINER |
|------------------------|
| SHAHNAN SHAH, KHATOL S |

| ART UNIT | PAPER NUMBER |
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| 1645 | |

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| 02/04/2008 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/781,499

Applicant(s)

CHATEAU ET AL.

Examiner

Khatol S. Shahnan-Shah

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/ are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 9/14/2007 has been entered. Claims 15-21 have been canceled. Claim 2 has been amended.
2. Claims 1-14 are pending and under consideration.

Information Disclosure Statement

3. The information disclosure statement filed 10/1/6/2007 has been acknowledged. Applicants have mentioned enclosing of international search report of application WO2004/076659 with said correspondence. This office has not received said search report.

Rejections Withdrawn

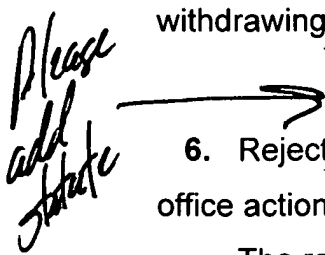
4. Rejection of claims 1-14 under 35 U.S.C. 101 double patenting rejection, made in paragraph 7 of office action mailed 1/18/2007 is withdrawn due to withdrawing of claims 1-5 and 7-11 of copending application 10/546,139.
5. Rejection of claim 6 under non-statutory obviousness- type double patenting rejection, made in paragraph 9 of office action mailed 1/18/2007 is withdrawn due to withdrawing of claims 1 and 6 of copending application 10/546,139.

Rejections Maintained

6. Rejection of claims 1-4 and 8-14 under 35 U.S.C. 102 (b), made in paragraph 12 of office action mailed 1/18/2007 is maintained.

The rejection was stated below:

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Claims 1-4 and 8-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamori et al. (Applied Microbial Biotechnology, vol.52, pp. 179-185, 1999).

The claims are drawn to a method for the preparation of evolved microorganisms permitting a modification of metabolic pathways, comprising the following steps: a) preparing a modified microorganism by genetic modification of cells of an initial microorganism so as to inhibit the production or consumption of a metabolite when that microorganism is grown on a defined medium, thereby impairing the ability of that microorganism to grow; b) culturing the modified microorganism thereby obtained on said defined medium to cause it to evolve, where the defined medium can contain a co-substrate to allow such evolution; and c) selecting a modified microorganism able to grow on said defined medium, if necessary with a co-substrate.

Nakamori et al. teach a preparation of evolved microorganisms permitting a modification of metabolic pathways (see abstract). Nakamori et al. teach preparing a modified microorganism by genetic modification of cells of an initial microorganism so as to inhibit the production or consumption of a metabolite (methionine) when that microorganism is grown on a defined medium, see page 180 wherein E.coli JM 109 cells in the late exponential phase in LB medium were mutagenized. Nakamori et al. produced L-methionine-analogue resistant mutants (see page 180). Nakamori et al. teach culturing the modified microorganism thereby obtained on said defined medium to cause it to evolve, where the defined medium can contain a co-substrate to allow such evolution and c) selecting a modified microorganism able to grow on said defined medium, if necessary with a co-substrate, see page 180 under selection and cultivation of L-methionine-producing mutants (i.e. an evolved microorganism). Nakamori et al teach biosynthesis pathway of amino acids and methionine (see title and abstract).

Nakamori et al. also teach limitation of claims 8-14 wherein the evolved microorganism possesses at least one evolved gene coding for an evolved protein (see page 182 Introduction of the wild-type metJ gene into the L- methionine-producing strain with a mutant metJ gene and page 183 Molecular modeling of the DNA-binding region in the mutant MetJ protein). The prior art anticipates the claimed invention.

Applicants' arguments filed 9/14/2007 have been fully considered but they are not persuasive.

Applicants argue:

- Nakamori Does Not Teach The Elements of the Claim.

In the Office Action, the Office has incorrectly recited the elements of the claims and identified elements in the cited references that are absent.

Specifically, in the instant Action, the Office characterizes the claims as:

permitting a modification of metabolic pathways comprising the following steps:

a) preparing a modified microorganism by genetic modification of cells of an initial microorganism so as to inhibit the production or consumption of a metabolite when that microorganism is grown on a defined medium, thereby impairing the ability of that microorganism to grow;

b) culturing the modified microorganism thereby obtained on said defined medium to cause it to evolve, where the defined medium can contain a co-substrate to allow such evolution; and c) selecting a modified microorganism able to grow on said defined medium, if necessary with a co-substrate.

- Nakamori et al. do not Disclose Directed Genetic Modification.
- Nakamori et al. do not obtain a Modified Microorganism which is then Cultured.

In response to applicants' arguments the office brings applicants attention to the instant specification (see page 3) following definitions:

Evolved microorganism as according to the invention an 'evolved microorganism' is defined as a microorganism obtained by selection of a modified microorganism.

The evolved microorganism displays at least one difference from the modified

microorganism. This difference may, for example, be the improvement of an enzymatic characteristic, or the creation of a new metabolic pathway.

According to the invention a '**metabolic pathway**' is one or more enzymatic reactions the succession of which forms a molecule (product) that is different from the starting molecule (substrate).

According to the invention a '**modification**' is a change, in **particular a deletion**, of at least one gene and/or its promoter sequence, which gene codes for an enzyme.

According to the invention a '**metabolite**' is a molecule synthesized and/or transformed by the microorganism.

Page 6 further recites "According to the invention a 'modified microorganism' is a microorganism obtained by performing controlled modifications, i.e., that are not the result of a process of evolution. Examples of such a modification are the **directed mutation or deletion of a gene, or the directed modification of a promoter**.

Therefore, according to applicants own definitions Nakamori et al. do teach a preparation of evolved microorganisms by modifying a metabolic pathways (see abstract). Nakamori et al. teach preparing a **modified microorganism by genetic modification of cells of an initial microorganism** so as to inhibit the production or consumption of a **metabolite (methionine)** when that microorganism is grown on a defined medium, see page 180 wherein E.coli JM 109 cells in the late exponential phase in LB medium were mutagenized. Nakamori et al. produced L-methionine-analogue resistant mutants (see page 180). Therefore, Nakamura's mutation does result in a specific mutation in metabolic pathway. Nakamori et al. do teach **Directed Genetic Modification and Modified Microorganism which is then Cultured**. Nakamori et al. teach preparing a modified microorganism by genetic modification of cells of an initial microorganism so as to inhibit the production or consumption of a metabolite (methionine) when that microorganism is grown on a defined medium, see page 180 wherein E.coli JM 109 cells in the late exponential phase in LB medium were mutagenized. Nakamori et al. produced L-methionine-analogue resistant mutants (see page 180). Nakamori et al. teach culturing the modified microorganism thereby obtained on said defined medium to cause it to evolve, where the defined medium can contain a co-substrate to allow such evolution and

c) selecting a modified microorganism able to grow on said defined medium, if necessary with a co-substrate, see page 180 under selection and cultivation of L-methionine-producing mutants (i.e. an evolved microorganism).

7. Rejection of claims 1-7 under 35 U.S.C. 102 (b), made in paragraph 13 of office action mailed 1/18/2007 is maintained.

The rejection was as stated below:

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/177112 published 2 September 1993.

The claims are drawn to a method for the preparation of evolved microorganisms permitting a modification of metabolic pathways, comprising the following steps: a) preparing a modified microorganism by genetic modification of cells of an initial microorganism so as to inhibit the production or consumption of a metabolite when that microorganism is grown on a defined medium, thereby impairing the ability of that microorganism to grow; b) culturing the modified microorganism thereby obtained on said defined medium to cause it to evolve, where the defined medium can contain a co-substrate to allow such evolution; and c) selecting a modified microorganism able to grow on said defined medium, if necessary with a co-substrate.

WO 93/177112 teaches a preparation of evolved microorganisms permitting a modification of metabolic pathways i.e. biosynthesis pathway of amino acids (see abstract and amended claims). WO 93/177112 teaches preparing a modified microorganism by genetic modification of cells of an initial microorganism so as to inhibit the production or consumption of a metabolite (methionine) when that microorganism is grown on a defined medium (see claims). WO 93/177112 teaches preparing a modified microorganism by genetic modification of cells of an initial microorganism see amended claim 1. WO 93/177112 teaches culturing the modified microorganism thereby obtained on said defined medium to cause it to evolve, where the defined medium can contain a co-substrate to allow such evolution and c) selecting a modified microorganism able to grow on said defined medium, if necessary with a co-substrate, see claims specially claim 1. WO 93/177112 teaches limitations of claims 5-7 wherein the metabolic pathway consumes

NADPH (see figure 1). WO 93/177112 teaches biosynthesis pathway of amino acids, methionine (see title and abstract). The prior art anticipates the claimed invention.

Applicants' arguments filed 9/14/2007 have been fully considered but they are not persuasive

Applicants argue:

- WO 93/177112(Lievense) Does Not Teach Preparing a Modified Microorganism that is Impaired in Its Ability To Grow

The present invention teaches a directed genetic modification which results in a modified organism having a genetic modification "thereby impairing the ability of that microorganism to grow". The introduced deficiency is complimented organically in order to rescue the modified microorganism. In contrast, WO 93/177112(Lievense) merely inserts foreign genes in bacteria allowing the bacteria to used non-native substrates to produce methionine. The growth of the transformed bacteria taught by Lievense is not impaired.

In response to applicants' arguments the office brings applicants attention to the instant specification (see page 3) following definitions:

evolved microorganism as according to the invention an '**evolved microorganism**' is defined as a microorganism obtained by selection of a modified microorganism.

The evolved microorganism displays at least one difference from the modified microorganism. This difference may, for example, be the improvement of an enzymatic characteristic, or the creation of a new metabolic pathway.

According to the invention a '**metabolic pathway**' is one or more enzymatic reactions the succession of which forms a molecule (product) that is different from the starting molecule (substrate).

According to the invention a '**modification**' is a change, in **particular a deletion**, of at least one gene and/or its promoter sequence, which gene codes for an enzyme.

According to the invention a '**metabolite**' is a molecule synthesized and/or transformed by the microorganism.

Page 6 further recites, "According to the invention a 'modified microorganism' is a microorganism obtained by performing controlled modifications, i.e., that are not the result of a process of evolution. Examples of such a modification are the **directed mutation or deletion of a gene, or the directed modification of a promoter.**

Therefore, according to applicants own definitions WO 93/177112 teaches a preparation of evolved microorganisms permitting a **modification of metabolic pathways i.e. biosynthesis pathway of amino acids** (see abstract and amended claims). WO 93/177112 teaches preparing a **modified microorganism by genetic modification** of cells of an initial microorganism so as to inhibit the production or consumption of a **metabolite** (methionine) when that microorganism is grown on a defined medium (see claims). As to applicants arguments that WO 93/177112 only teaches enhancement not inhibition.

In response applicants' attention is drawn to the language of the WO 93/177112 abstract "and/or by modifying the methionine biosynthetic pathway" when a reduced sulfur source is used in the medium production of methionine is enhanced and when an oxidized sulfur source is used production of methionine is inhibited (see table 1, page 7).

Status of Claims

8. No claims are allowed.

Claims 1-14 stand rejected.

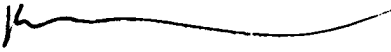
Conclusion

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Art Unit: 1645

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on Mondays and Wednesdays from 12:30-6:30 PM and Thursdays from 12:30-4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898.


The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Khatol Shahnan-Shah

Art Unit 1645

January 28, 2008



SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600